Acute Kidney Injury in the Pregnant Patient

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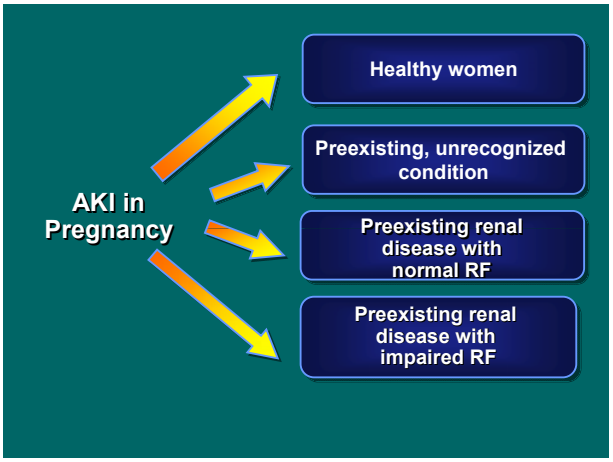
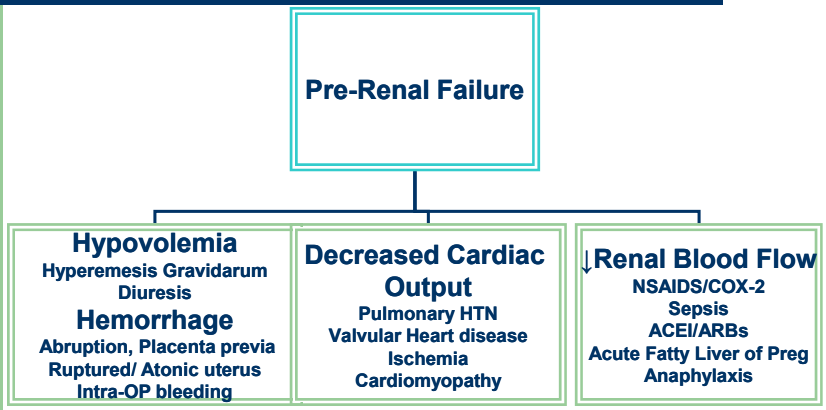
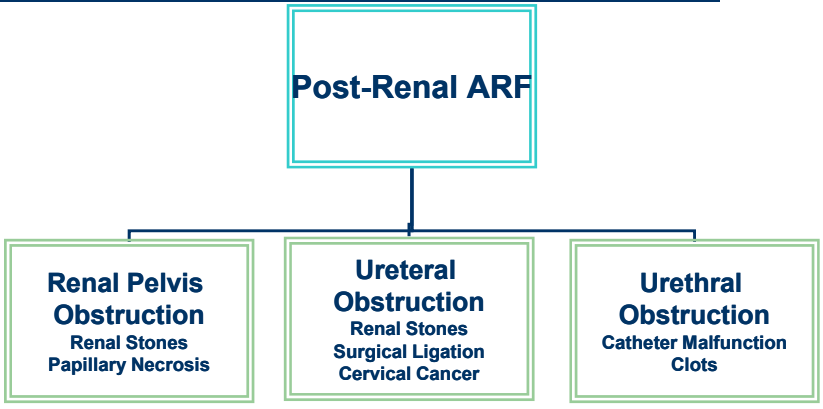
AKI in Pregnancy



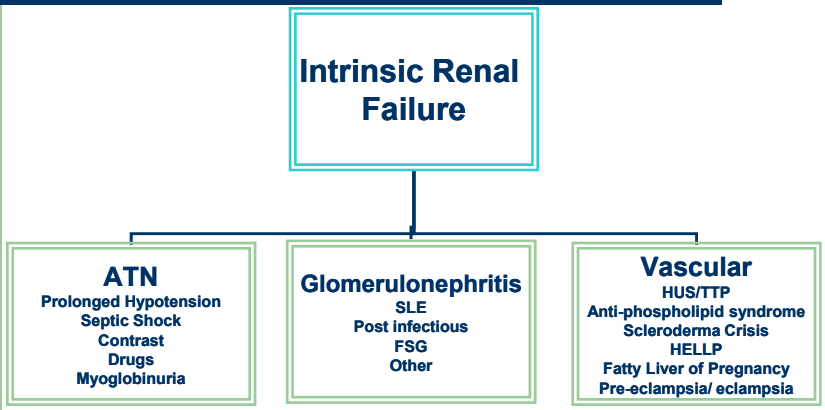
ARF in Pregnancy



ARF in Pregnancy



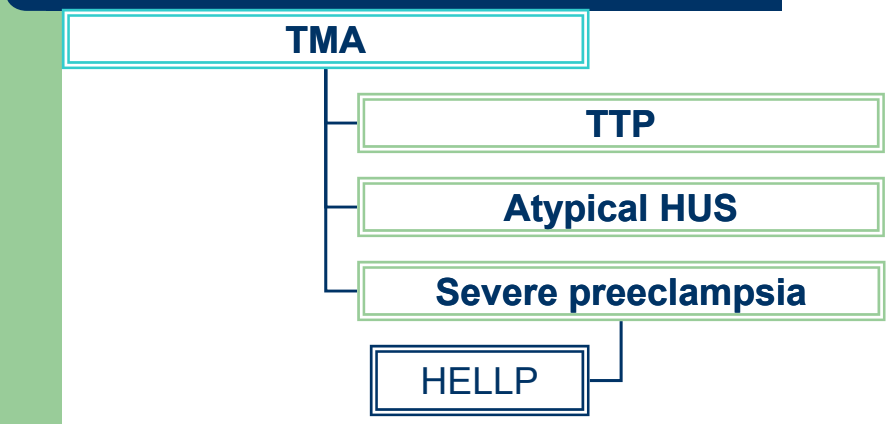
ARF in Pregnancy



Case 1: Thrombotic microangiopathy and pregnancy

- 43-year old, first, twin pregnancy (IVF) admitted at 33 week gestation for increasing edema and decreased urinary output
- Lab results: AST 636 u/l, ALT 398 u/l, LDH 1288 u/l, Cr 2.7 mg/dL, thrombocytopenia
- DX: HELLP syndrome Urgent C-section
  - Hemorrhagic shock, multiple transfusions, platelets, FFP, plasmapheresis

Thrombotic microangiopathy (TMA) in Pregnancy



Atypical HUS

- Excessive activation of the alternative C3 convertase leads to complement induced lesions, mainly endothelial cells
  - Acquired anti-Factor H antibodies
  - Constitutional, inactivating mutations in factors H and I, or membrane cofactor protein
  - Activating mutations in factor B or C3 coding genes (components of the alternative C3 convertase)

Atypical HUS

- Atypical HUS-non-shiga toxin related HUS- due to mutations in genes coding for proteins involved in the alternative complement pathway
- The alternative pathway is initiated spontaneously
- Plasma and membrane bound factors that down-regulate its activity: factor H, factor I, membrane cofactor protein, and decay-accelerating factor

Pregnancy-associated atypical HUS

- Atypical HUS in 100 adult female patients
  - Pregnancy-associated, n=21
- 79% presented postpartum
- Moderate thrombocytopenia (>100K in 40%)
- No neurological signs/symptoms
- Renal biopsy (8/21):Arteriolar and capillary thrombi, “double contour,”mesangiolysis
- Alternative complement pathway gene mutations in 18 of the 21
  - 76% ESRD by last follow-up
-

Fakhouri et al. JASN, 2010

Pregnancy associated atypical HUS

- At least 1 pregnancy before HUS, n=35
- Alternative pathway mutations: in 26/35 (74%)
- Complement abnormalities, n=44 (18+26): fetal loss (4.8%) and preeclampsia (7.7%)
- Postpartum HUS may be due to loss of placental regulatory proteins that compensate for increased complement activation due to inherited mutations

Fakhouri et al. JASN, 2010

Case 1: Thrombotic microangiopathy and pregnancy

- Renal biopsy: TMA
- ADAMTS 13 levels 45-68%, normal C3, C4, CH50, factor H and I, absent factor H antibody
- Negative mutation analyses
- Positive Lupus anticoagulant
- On chronic HD; evaluated for a RT

Differential diagnosis: PE/HELLP vs. HUS/TTP

	Preeclampsia	HUS	TTP
Time of onset	late 3rd trimester	postpartum	2nd and 3rd
Renal failure	unusual	common	minimal or absent
Renal prognosis	recovery	75% ESRD	fair
Neurological findings	present	minimal or absent	dominant
Low platelet count	present (HELLP)	present	present
DIC	present	absent	absent
Abnormal LFT	present (HELLP)	absent	absent
Complement alternative pathway	present (HELLP)	present	absent
↓ ADAMTS13	mild to moderate	absent	severe

Pregnancy in Patients with Preexisting Renal Disease

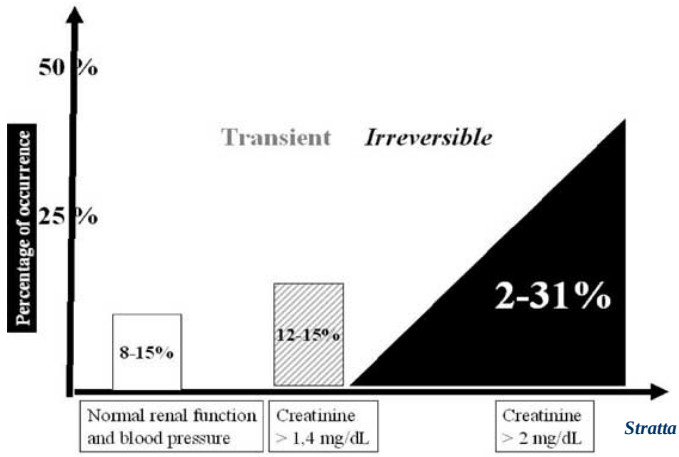
- The most important determinant of progression of renal insufficiency is renal function at the time of conception
- Possible contributing factors
  - Hypertension
  - ↑ Proteinuria during pregnancy
  - Urinary tract infections

Pregnancy in Patients with Preexisting Renal Disease

Pregnancy and progression of renal insufficiency

- No adverse effect with **Cr<1.4 mg/dL** and normal BP
- ↑progression if **Cr≥1.4 mg/dL,** including patients with DM nephropathy
- **Cr≥3.0 mg/dL:** pregnancy losses and maternal morbidity

Risk of Worsening of Renal Function in Pregnancy by GFR



Stratta et al; 2006

Pregnancy in Patients with Preexisting Renal Disease

Type of disease, pregnancy and progression of renal insufficiency

- More likely in MPGN, FSG and reflux nephropathy
- Lupus nephritis: ↓ risk of exacerbation if in remission for ≥ 6 months

Pregnancy in Patients with Preexisting Renal Disease

- Spontaneous abortions 8%
- Prematurity 19%
- Perinatal loss 13%

Jungers, 1997

- Preeclampsia 30%
- IUGR 50%

Lupus Nephritis and Pregnancy

- 31 year old with SLE for 10 years, 6 weeks pregnant
- History of 2 miscarriages, DVT x 2
- Prior to pregnancy, maintained on Prednisone, Plaquenil, Coumadin

Lupus Nephritis and Pregnancy

- d/c Coumadin, Plaquenil
- Start
  - Dalteparin 13,000 IU
  - Aspirin 81 mg QD
- Continue Labetalol for HTN
- 12 weeks of gestation: SOB, CP
- CT chest: old thrombus

Lupus Nephritis and Pregnancy

- Negative Doppler US LE's
- Worsening proteinuria, HTN, Cr 1.6 from 1.0 mg/dL
- Nephrotic syndrome
- Kidney BX: membranous GN
- Prednisone↑to 60 mg, Plaquenil restarted 200 mg BID

Lupus Nephritis and Pregnancy

- 3 weeks later: local ER evaluation for SOB
- Cardiorespiratory arrest, resuscitated, Transferred to Mayo
- Intubated, Sedated, Oliguria develops- unresponsive to diuretics, volume overload.
- Renal replacement required...

Lupus Nephritis and Pregnancy

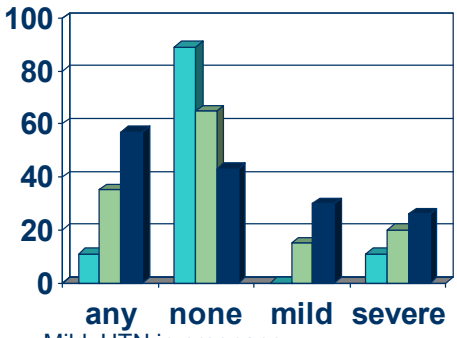
- CRRT was initiated, pressors required, pulse steroids
- Fetal demise documented
- Apnea test positive
- Support withdrawn

Lupus Nephritis and Pregnancy

- 58 patients with SLE and 90 pregnancies
- No renal involvement (n=47)
- Quiescent LN (n=20)
  - Proteinuria <0.5 mg/24 hrs and inactive sediment
- Active LN (n=23)
  - Proteinuria >0.5 mg/24 hrs and/or active sediment
- LN biopsy confirmed in 19/26 patients
  - 1 Type II Mesangial
  - 8 Type III Focal Segmental Proliferative
  - 7 Type IV Diffuse Proliferative
  - 3 Type V Membranous

Garovic et al. Lupus 2009

Maternal Outcomes



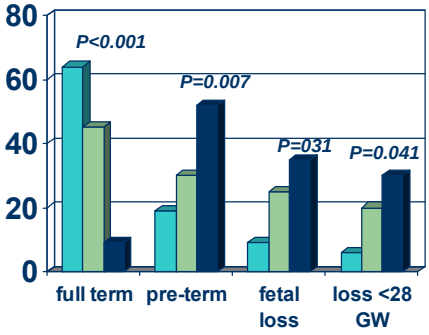
P<0.001

- SLE w/o LN
- Quiescent LN
- Active LN

Mild: HTN in pregnancy
Severe: preeclampsia, eclampsia, stroke, HELLP, and death

Garovic et al. Lupus 2009

Fetal Outcomes



- SLE w/o LN
- Quiescent LN
- Active LN

Fetal loss: therapeutic/ spontaneous Ab, or stillbirth

Garovic et al. Lupus 2009

Systematic Review and Meta-Analysis of Pregnancy Outcomes in Patients with SLE and LN

- 37 studies with 1842 patients and 2751 pregnancies

Maternal complications

- Lupus flare, 25.6%
- Hypertension, 16.3%
- Nephritis, 16.1%
- Pre-eclampsia, 7.6%
- Eclampsia, 0.8%

Garovic et al. cJASN, 2010

Systematic Review and Meta-Analysis of Pregnancy Outcomes in Patients with SLE and LN

Fetal Complications

- Induced abortion rate, 5.9%
- Spontaneous abortion, 16.0%
- Stillbirth, 3.6%
- Neonatal deaths, 2.5%
- IUGR, 12.7%
- Unsuccessful pregnancy rate, 23.4%
- Premature birth rate, 39.4%

Garovic et al. cJASN, 2010

Systematic Review and Meta-Analysis of Pregnancy Outcomes in Patients with SLE and LN

Meta-regression analyses

- Positive associations between premature birth rate and active nephritis
- Increased hypertension rates in subjects with active nephritis or a history of nephritis
- History of nephritis was associated with pre-eclampsia
- Anti-phospholipid antibodies were associated with hypertension, premature birth, and an increased rate of induced abortion

Garovic et al. cJASN, 2010

Pregnancy in Patients with Preexisting Renal Disease: Summary

Good prognosis: remission, no proteinuria or HTN (or controlled on meds)

Risk factors for complications of pregnancy:

- ↓ GFR
- Hypertension
- Nephrotic range proteinuria
- Advanced maternal age
- Underlying disease: poorly controlled DM, active SLE